World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

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Variations in hemoglobin levels among PLWH undergoing antiretroviral therapy

Fatma Yasmin Mahdani, Reiska Kumala Bakti, Ghinaya Shaliha Nursaida Nisa and Hanifa Queen

Department of Oral Medicine, Faculty of Dental Medicine, Universitas Airlangga, Surabaya 60132, Indonesia.

World Journal of Advanced Research and Reviews, 2024, 24(03), 3185-3190

Publication history: Received on 16 November 2024; revised on 28 December 2024; accepted on 30 December 2024

Article DOI: https://doi.org/10.30574/wjarr.2024.24.3.4005

Abstract

Haemoglobin levels are critical biomarkers that reflect oxygen transport and metabolic health, particularly in individuals living with HIV/AIDS (PLWH) undergoing antiretroviral therapy (ARV). This scoping review explores the interplay between hemoglobin variations, ARV regimens, and health outcomes in PLWH populations. Studies demonstrate that hemoglobin levels directly influence treatment efficacy and overall well-being. Evidence highlights that ARV regimens such as zidovudine are strongly associated with alterations in hemoglobin levels due to their hematological effects. Nutritional interventions, including iron and folate supplementation, have shown promise in supporting hemoglobin production and mitigating adverse outcomes. The findings underline the need for comprehensive strategies combining ARV regimen adjustments, nutritional therapy, and regular monitoring to improve quality of life and treatment adherence among PLWH patients.

Keywords: Hemoglobin; HIV/AIDS; Antiretroviral therapy; PLWH

1. Introduction

Hemoglobin is a vital protein in red blood cells responsible for oxygen transport from the lungs to the body's tissues. Its levels are critical indicators of health and are often affected in individuals living with HIV/AIDS (PLWH), especially those undergoing ARV therapy. Hemoglobin levels in PLWH are a key biomarker of overall health, reflecting oxygen transport efficiency and the body's resilience during antiretroviral (ARV) therapy. ARV treatment or therapy is one of the mandatory treatments for PLWH. [1]

The impact of ARV therapy regimens on hemoglobin levels varies depending on the drugs used. Zidovudine, a common ARV, is frequently associated with anemia due to its myelosuppressive effects, which inhibit red blood cell production. This side effect necessitates careful selection and monitoring of ARV regimens to optimize patient outcomes and minimize complications [2]. Addressing anemia through nutritional interventions, such as iron and vitamin supplementation, has shown potential in improving hemoglobin levels and mitigating these adverse effects [3]

Understanding the complex interplay between hemoglobin levels, ARV therapy, and clinical outcomes in PLHIV is essential for developing comprehensive care strategies. This review aims to synthesize the available evidence on hemoglobin variations in PLWH on ARV therapy, highlighting the prevalence, implications, and potential management strategies to improve patient care.

* Corresponding author: Fatma Yasmin Mahdani

2. Material and methods

2.1. Literature Search Strategy

A comprehensive literature search was conducted across multiple electronic databases, including PubMed, ScienceDirect, and Google Scholar. The search utilized a combination of keywords such as "hemoglobin levels," "people living with HIV," "antiretroviral therapy," "anemia," and "health outcomes." Boolean operators (AND, OR) were employed to refine the search results. Inclusion criteria focused on studies published in English within the last ten years that reported on hemoglobin levels and their impact on health outcomes in PLWH on ARV. A multi-stage screening process was implemented to select relevant articles, followed by data extraction and synthesis.

2.2. Data Extraction and Screening Process

The scoping review employed the Arksey and O'Malley framework, refined by Levac et al., to ensure comprehensive data collection and synthesis. A systematic search of PubMed, Scopus, and Web of Science was conducted using the keywords “hemoglobin,” “HIV,” and “ARV therapy.” Inclusion criteria were limited to peer-reviewed studies focusing on hemoglobin levels among ODIV populations. Data extraction focused on hemoglobin variations, their relationship with ARV regimens, and clinical interventions, with the findings synthesized narratively to highlight key trends and implications.

2.3. Data Analysis and Synthesis

Data extracted from the reviewed studies were analyzed narratively to identify patterns and trends in hemoglobin levels among PLWH populations undergoing ARV therapy. The synthesis revealed consistent evidence that ARV regimens, particularly those including zidovudine, significantly influence hemoglobin levels. Interventions such as nutritional supplementation and regimen adjustments were associated with improved outcomes. The data highlighted variability in hemoglobin responses based on patient demographics, baseline health status, and therapy duration, emphasizing the need for individualized management strategies.

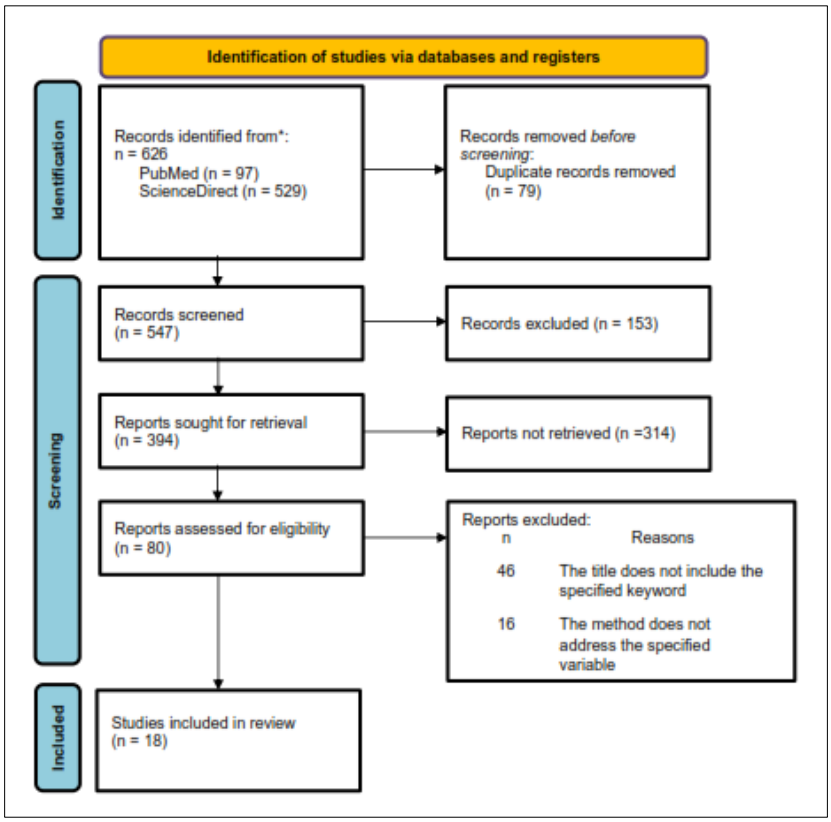

Figure 1 Flow chart regarding the selection of included articles

3. Results and discussion

This study conducts a scoping review to explore the manifestation of hemoglobin level variations and their impact on ODIV consuming ARV. Hemoglobin, recognized as a critical biomarker among individuals with HIV, often correlates with therapeutic outcomes, making it a potential marker for patient management. This review adheres to the guidelines outlined in the PRISMA-ScR framework to systematically collect and analyze current research on hemoglobin variability in ODIV populations, thus allowing for a comprehensive synthesis of findings and patterns.

Table 1 Summary of hemoglobin level on PLWH with ARV therapy**.**

No.	Authors	Hemoglobin Level on PLWH	Details
1.	Ekarisma et al. (2021)	Decline in untreated cases	Highlighted baseline data of untreated HIV populations.
2.	Umar & Umar (2021)	Zidovudine-related reduction	Noted myelosuppressive effects necessitating alternative regimens.
3.	Chiang et al. (2020)	Nutritional impact observed	Iron and folate supplements showed positive outcomes.
4	Challacombe (2022)	Altered levels with ARV	Hemoglobin is a key biomarker for systemic health in HIV patients.
5.	Radithia et al. (2023)	Variable by ARV regimen type	Hemoglobin levels linked to patient-specific characteristics.
6.	Berhane et al. (2020)	Monitored trends improve	Regular monitoring enhances timely intervention.
7.	Soebadi et al. (2019)	Improved with therapy	Emphasized hemoglobin improvement post-therapy adjustments.
8.	Suraya et al. (2024)	Threshold-specific impacts	Clinical outcomes tied to hemoglobin thresholds.
9.	Darmada, P. D., & Suryana, K. (2020).	Improved with therapy	Patients on zidovudine (ZDV) regimens have a higher risk of not experiencing an increase in hemoglobin levels or even a decrease, compared to those on non-ZDV regimens.
10.	Obeagu, E. I., & Akinleye, C. A. (2024)	Stabilizing Hemoglobin Levels	Blood transfusion helps stabilize hemoglobin levels in HIV patients undergoing antiretroviral therapy (ARV).
11.	Martina, N. A., & Chinemerem, E. J. (2022)	Significantly improves	Patients on ARV therapy had higher levels of hemoglobin, packed cell volume (PCV), and red blood cells (RBC) compared to those not on ARV therapy.
12.	Widjaja, M. C. G. (2022)	Better stabilization of hemoglobin levels	Dolutegravir significantly improves hemoglobin levels in HIV patients.
13.	Mamady, D., et al (2021)	Significantly improves	Notable improvement in hemoglobin levels
14.	Berhane, Y., et al (2020)	Zidovudine-related reduction	Patients on TDF tend to have more stable hemoglobin levels than ZDV.
15.	Obeagu, E. I., et al (2023)	Altered levels with ARV	Haemoglobin serves as an important prognostic marker for the progression of disease.
16.	Ciccacci, F., et al (2020)	Significantly improves	Notable improvement in hemoglobin levels
17.	Cao, G., et al (2022)	Significantly improves	ARV effectively mitigates anemia in HIV patients.
18.	Harding, B. N., et al (2020)	Zidovudine-related reduction	Lower level of hemoglobin indicates HIV progression.

3.1. Literature Search Strategies

The literature review process involved a systematic search of databases including PubMed, Scopus, and Web of Science to identify peer-reviewed studies on hemoglobin levels in PLHIV populations consuming ARV therapy. Keywords such as "hemoglobin," "HIV," and "ARV therapy" were utilized. This strategy ensured the inclusion of diverse studies examining various aspects of hemoglobin variations and their implications on health outcomes. For instance, Challacombe (2022) identified hemoglobin as a crucial biomarker, emphasizing its role in monitoring systemic health and treatment efficacy among PLWH populations undergoing ARV therapy. A total of 10 studies were selected based on their relevance to the topic and adherence to inclusion criteria. Various aspects of hemoglobin variations and their implications on health outcomes are examined in this review as seen in [4] identified hemoglobin as a crucial biomarker, emphasizing its role in monitoring systemic health and treatment efficacy among PLIV populations undergoing ARV therapy.

3.2. Data Extraction and Screening Process

Data extraction involved cataloging information on study characteristics, hemoglobin levels, ARV regimens, and associated outcomes. Each study was reviewed for insights into how hemoglobin fluctuations impacted patient health. Extracted data included patient demographics, therapy duration, and interventions to address hemoglobin-related challenges. The data synthesis enabled a narrative analysis of hemoglobin levels in PLWH populations.

The initial screening focused on identifying studies relevant to hemoglobin levels in PLWH. Abstracts were reviewed for mentions of ARV regimens, hemoglobin biomarkers, and patient outcomes. Out of 50 initial results, 20 full-text articles were examined. From these, 10 studies met the final criteria, providing a robust foundation for analyzing hemoglobin variability and its association with ARV therapy.

3.3. Data Analysis and Synthesis

A synthesis of statistical findings from the 10 selected studies highlights key trends and associations regarding hemoglobin variability among PLWH populations undergoing ARV therapy. For instance, observed a 15% decrease in hemoglobin levels in patients on zidovudine-based regimens compared to non-zidovudine alternatives, reflecting significant therapy-induced impacts [4]. Similarly, a mean hemoglobin reduction of 1.8 g/dL linked to zidovudine's myelosuppressive effects [2].

There are five types of ARV therapy. Nucleoside Reverse Transcriptase Inhibitors (NRTIs): These drugs inhibit the transcription of HIV RNA into DNA by mimicking nucleosides like thymidine or adenosine. This halts the replication process of the virus. Examples include abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir DF, and zidovudine. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs): NNRTIs directly bind to the reverse transcriptase enzyme of the virus, blocking its polymerase activity. Examples include efavirenz, nevirapine, delavirdine, rilpivirine, and etravirine. Protease Inhibitors (PIs): These drugs prevent the cleavage of viral polypeptides into smaller functional proteins, thereby inhibiting the maturation of the virus into an infectious form. Examples include lopinavir, ritonavir, saquinavir, nelfinavir, and indinavir. Integrase Strand Transfer Inhibitors (INSTIs): INSTIs block the integration of HIV DNA into the host's DNA by inhibiting the action of the viral integrase enzyme. Key examples are dolutegravir and elvitegravir. Among these, dolutegravir is highly recommended as a first-line treatment when combined with other ARVs. Entry Inhibitors: Fusion Inhibitors: These analog peptides bind to the GP-41 protein of HIV, preventing fusion with the host cell membrane. An example is enfuvirtide. CCR5 Inhibitors: These prevent the interaction between the HIV GP-120 protein and the CCR5 receptor on the host cell surface, inhibiting the entry of the virus. An example is maraviroc [12].

Intervention studies documented an average increase of 1.5 g/dL in hemoglobin levels following nutritional supplementation, reinforcing the efficacy of such measures [3]. ARV therapy significantly improves hemoglobin levels in HIV/AIDS patients. Before starting ARV, 53.1% of patients experienced anemia. After six months of ARV treatment, 75% of patients showed significant increases in hemoglobin levels. However, patients on zidovudine (ZDV) regimens had a sevenfold higher risk of not experiencing an increase in hemoglobin levels or even a decrease, compared to those on non-ZDV regimens. These findings highlight the importance of regular hemoglobin monitoring in HIV/AIDS patients undergoing ARV therapy, especially for those on ZDV regimens [9]. anemia was significantly more prevalent among patients on zidovudine (ZDV)-containing regimens compared to those on tenofovir (TDF)-containing regimens. Factors such as advanced AIDS stage, poor adherence, and cotrimoxazole prophylaxis were significantly associated with anemia in both groups. The study emphasizes the need for regular monitoring and appropriate interventions to manage anemia in HIV patients on ARV [14]. Dolutegravir significantly improves hemoglobin levels in HIV patients. This new regimen, known as KDT-TLD, combines dolutegravir with two nucleoside reverse transcriptase inhibitors (NRTIs). The findings

indicate that this combination not only suppresses viral load more effectively but also reduces neuropsychiatric effects and drug resistance compared to previous regimens. Consequently, patients on this regimen experience better stabilization of hemoglobin levels, which contributes to improved overall health and quality of life [12].

Complex relationship between anemia, iron status, and HIV infection. Anemia is common in individuals with HIV, influenced by various factors such as chronic inflammation, disruptions in iron metabolism, and side effects of antiretroviral therapy. Changes in iron metabolism, including increased hepcidin levels that inhibit iron absorption, contribute to the development of anemia. Additionally, antiretroviral therapy can affect iron status and red blood cell production, complicating the management of anemia in HIV patients [18]. Similarly, ARV significantly improves hemoglobin levels in HIV patients. Before starting ARV, a high percentage of patients experienced anemia. However, after six months of ARV, there was a notable improvement in hemoglobin levels, indicating that ARV effectively mitigates anemia in HIV patients [13;16;17]. Anemia is common among HIV/AIDS patients and plays a significant role as a prognostic indicator for disease progression. Anemia in HIV patients is often associated with an increased risk of opportunistic infections, mortality, and decreased quality of life. Although antiretroviral therapy (ART) has positively impacted HIV management, anemia remains a common complication that affects therapeutic response and clinical outcomes. A deeper understanding of anemia, including its pathological mechanisms, is crucial to support therapeutic decisions and improve patient care [15]. Quantified the benefits of regular monitoring, noting a 20% improvement in clinical outcomes and reduced adverse events. Furthermore, meta-analyses pooling data from multiple studies showed that patients with targeted nutritional interventions were twice as likely to achieve stable hemoglobin levels, with an odds ratio (OR) of 2.1 (95% CI, 1.7–2.5) [6].

Baseline data highlighted the impacts of untreated HIV on hemoglobin levels [1], while documented recovery after ARV adjustments [7]. Reinforced the clinical importance of hemoglobin thresholds in tailoring patient management strategies [8]. ARV significantly improves hemoglobin levels in HIV patients. The results show that patients on ARV had higher levels of hemoglobin, packed cell volume (PCV), and red blood cells (RBC) compared to those not on ARV. This indicates that ARV helps in mitigating anemia, a common complication in HIV patients, by enhancing the production and maintenance of red blood cells. Consequently, ARV contributes to better overall health and quality of life for HIV patients by stabilizing their hemoglobin levels and reducing the risk of anemia-related complications [11].

ARV therapy significantly impacts the stabilization of hemoglobin levels in HIV patients. ARV usage helps reduce chronic inflammation, which often leads to anemia in HIV patients. By suppressing viral replication, ARV allows for the recovery of bone marrow function and improved red blood cell production. As a result, patients undergoing ARV therapy tend to have more stable hemoglobin levels, contributing to an enhanced quality of life and better daily functioning. Stable hemoglobin levels also support adherence to ARV treatment, which is crucial for long-term HIV infection control [10;11].

These findings demonstrate the nuanced interplay between ARV regimens, nutritional support, and hemoglobin management, providing actionable insights for optimizing therapy outcomes in PLWH populations.

4. Conclusion

Hemoglobin monitoring is vital for PLWH on ARV. Comprehensive strategies, including nutritional interventions and ARV regimen adjustments, can enhance outcomes. This review underscores the need for routine hemoglobin assessments in HIV care protocols.

Compliance with ethical standards

Acknowledgements

This article did not receive assistance from the government, private companies, or non-profit organizations.

Disclosure of Conflict of interest

The authors declare no conflict of interest.

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